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Changes in the Latency of the Maximum Positive Peak of Visual Evoked Potential during Anesthesia

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Summary

The relationship between the latency of visual evoked potential (VEP) and the anesthetic concentration was investigated in surgical patients in order to examine the applicability of VEP in monitoring of the depth of anesthesia. The VEP was recorded with a standard EEG electrode from the midline parietal region in reference to both earlobes linked to the ground. An array of light-emitting-diodes mounted in opaque goggles was used to stimulate both eyes simultaneously and photic stimuli were delivered at random inter-pulse intervals with uniform distribution ranging from 2 to 5 seconds. Fifty trials of data were averaged to estimate that Pmax latency, i.e., the latent period from the photic stimulus to the maximum positive peak arising after 170 msec.

Increases in the Pmax latency following the administration of anesthetics and restorations to preanesthetic values after recovery from anesthesia were found. A significant correlation was demonstrated between the Pmax latency and the inspiratory concentration of enflurane. The latency of the Pmax showed a drastic and a sensitive prolongation from about 200 msec in the awake state up to about 600 msec at the stage where the EEG exhibits large-voltage slow waves. Thus the measurement of the Pmax latency of VEPs was found to be useful for monitoring the depth of anesthesia.

Introduction

Recent developments in clinical neurophysiology and in EEG evaluation techniques have enabled EEG monitoring of cerebral functions in anesthesia under various conditions (Dripps et al., 1972; Takeshita and Shimoji, 1974; Pichlmayr et al., 1984)[4,13,15]. Correlations between changes in EEG and the depth of anesthesia have been investigated for various forms of anesthesia, surgery, and physiological conditions, so that continuous EEG recording during anesthesia is now regarded as a

Key words: Depth of anesthesia, Monitoring of anesthesia, Enflurane, Post-stimulus-latency, Visual evoked potential (VEP).
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routine procedure.

Recent advances in computerized techniques stimulated the application of sensory evoked potentials monitoring in anesthesia (NUWER, 1986)[11]. Effects of preanesthetic medication and anesthetics on the visual eveked potential (VEP) were considered by DOMINO (1967) with the view of clinical application[3]. UHL et al. (1980) investigated the effect of halothane anesthesia on VEP and observed an increase in the latency of the positive peak P1 (or P100) arising about 100 msec after the stimulus[16]. The P1 increased in latency from an average of 113.2 msec in the awake state to 133.9 msec at 1.13% end-tidal halothane concentration. CHI and FIELD (1986) observed an increase in the latency of P1 but a significant decrease in its amplitude in case of isoflurane anesthesia, whereas an increase of amplitude in the VEP during enflurane anesthesia was noticed by BURCHIEL et al. (1975)[1,2]. In these investigations different anesthetics caused different changes in VEP amplitudes but an increase in the latency was a common feature for almost all anesthetic drugs.

Effects of various forms of anesthesia on early components of evoked potentials such as the somatosensory evoked potential (SSEP) and the brainstem auditory evoked potential (BAEP) have also been investigated from several aspects. MCPHERSON et al. (1985) observed that isoflurane significantly decreases the amplitude and increases the latency of SSEP's components with latency shorter than 80 msec[7]. The same tendency was observed by PETERSON et al. (1986) for SSEPs with latency shorter than 40 msec for halothane, enflurane and isoflurane[12]. They therefore concluded that the changes in SSEPs are not useful for monitoring. MANNINEN et al. (1985) found that isoflurane significantly increases the latency of peaks III, IV, and V fo BAEP but causes no consistent change in the amplitude[6].

In addition to such variabilities in EP amplitudes, various types of artefacts may obscure true changes in EP due to anesthesia and cause some confusion in understanding the observed results. Therefore, further investigations are needed in order to utilize a relation between the VEP and the anesthetic concentration for monitoring of the depth of anesthesia.

In this paper, in contrast to previous observation concerning BSEPs or early components of SSEPs, and VEPs, we focus our attention to the VEP long latency components. In particular we examined the influence of anesthesia upon the latency of the maximum positive peak in VEPs (the Pmax latency) that appears about 170 msec after the stimulus which is well beyond the average latency of the maximum positive peak for unanesthetized normal subjects. A significant correlation was found between the anesthetic concentration and the prolongation of the Pmax latency. Thus a method based on estimating Pmax latency can be applied in monitoring of anesthesia. A special random pulse generator was used to trigger random photic stimuli in order to minimize the effects of background activity (NOGAWA et al., 1973, 1976)[9,10].

Method

Recording and averaging of eveoked potentials was performed with a Cadwell CA-5200 type instrument (Cadwell Laboratories, Inc., Washington USA). VEPs were recorded by means of a standard electrode at Pz with the reference electrode attached to linked pinnae. The photic stimulus was given to both eyes by an array of light-emitting-diodes (LED) mounted in opaque goggles (10 LEDs with 65 milli-candela each and flash duration of 5 msec). Stimuli were delivered randomly i.e., the inter-stimulus intervals had a uniform distribution in the range from 2 to 5 seconds. The maximal sample size averaged was 50 trials per measurement. By means of the Cadwell CA-5200 computer,

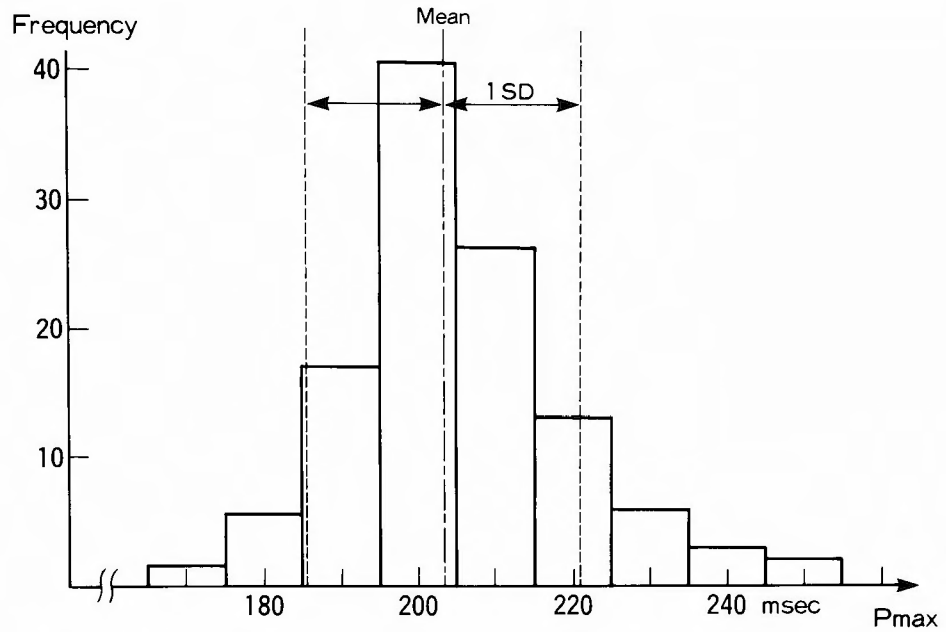

Fig. 1. Histogram of the Pmax latencies for unanesthetized normal subjects. Mean 203.2 msec, standard deviation 17.6 msec.
Results were obtained from 140 subjects.

the desired latency time was given in digital form.

In a preliminary control series of measurements, we observed the Pmax latency of the potential evoked by the LED stimulus on 140 unanesthetized normal subjects. As is shown in a histogram of Fig. 1, the observed Pmax latencies are distributed around the central value 203.2 msec with standard deviation ±17.6 msec; the range within one standard deviation (1SD) is 185.5–220.9 msec (106 examples out of 140 sugbjects; 75.7%) and within 2SD is 167.8–238.6 msec (132 out of 140; 94.3%). Therefore, we regard the Pmax latencies in the range 190–230 msec as 'normal', those in the range 170–190 msec or 230–250 msec as 'borderline', and those in the range below 170 msec or above 250 msec as 'abnormal'. Taking this result into account, we set the computer to measure latencies of the maximum positive peaks longer than 170 msec. A reason why we were concerned with the maximum peak is that it is more readily detected using a relatively small number of trials (less than 50 trials). A large number of trials (for example more than 500 trials) were required to find early components of VEPs.

The anesthetized subjects were patients under surgical operation. Nitrous-oxide with concentration ratio, for example, $O_2/N_2O = 2\ l/4\ l$ was used for every case. With or without preadministration of neuro-lepto-anesthesia (NLA) by means of droperidol, the anesthetics fentanyl, thiamylal, enflurane or halothane were applied under a semi-closed inspiratory system. Anesthetic concentration was changed as desired.

Results

Two typical effects of anesthetics on the Pmax latencies are shown in Figs. 2 and 3. The

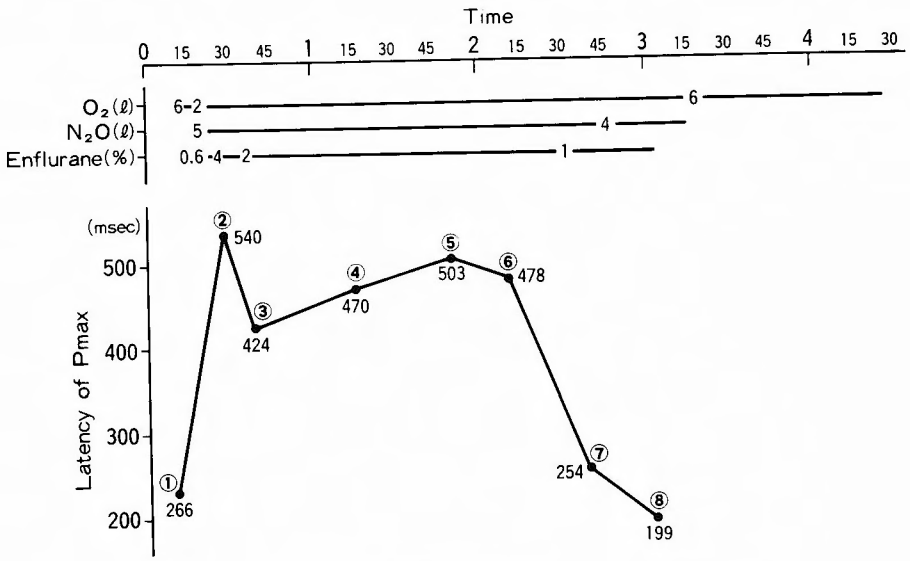

Fig. 2 (a)

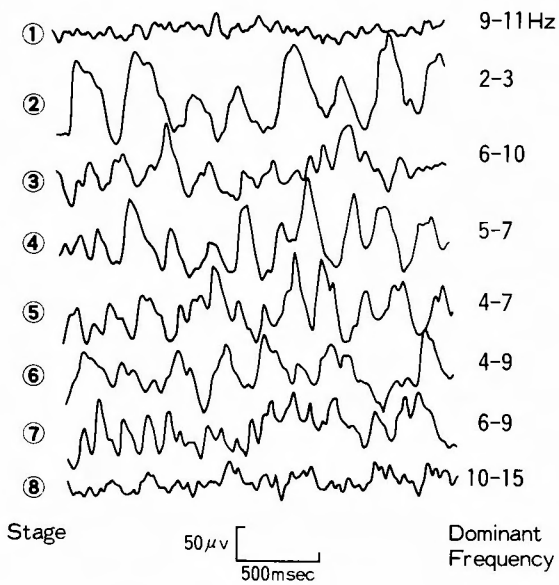

Fig. 2 (b)

Fig. 2. (a): Changes in the Pmax latency under intraoperative anesthesia. Types of anesthetic drugs and changes in time of their concentrations are shown at the side of the observed Pmax values. Enflurane with nitrous-oxide anesthesia. Patient: 39 year-old male, Cholecystectomy. ① preanesthesia. ② 3 minutes after 4% enflurne. ③ 5 minutes after 2% enflurane. ④ 40 minutes after 2% enflurane. ⑤ 80 minutes after 2% enflurane. ⑥ 100 minutes after 2% enflurane. ⑦ 10 minutes after 1% enflurane. ⑧ 10 minutes after turn-off of enflurane.

(b): Waveforms and dominant frequencies of ongoing EEG at corresponding stages.

changes in the Pmax latency of VEP along with the data concerning the anesthesia are given in part (a) and the EEG records at the different stages of anesthesia are shown in part (b).

Figure 2 shows a case for enflurane anesthesia. The patient was a 39 year-old male with body-weight 55 kg operated for Cholecystectomy. The Pmax latency in the preanesthesia period was 266

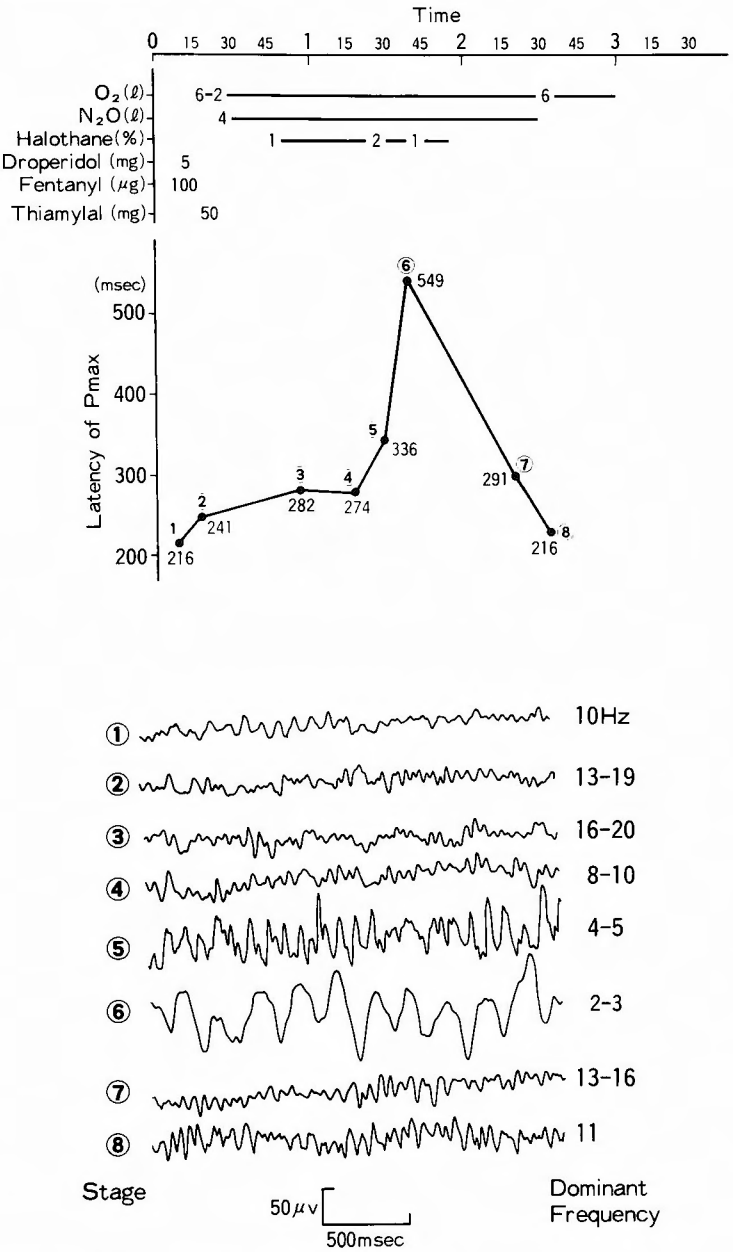

Fig. 3. The same as in Fig. 1 except for anesthesia (Halothane with NLA) and patient (56 year-old male, Cholecystectomy). ① preanesthesia. ② 5 minutes after administration of 5 mg droperidol and 100μg fentanyl. ③ 5 minutes after 1% halothane. ④ 25 minutes after 1% halothane. ⑤ 3 minutes after 2% halothane. ⑥ 10 minutes after 2% halothane. ⑦ 20 minutes after turn-off of halothane. ⑧ after awaking.

msec. Under 4.0% enflurane concentration together with nitrous-oxide anesthesia (concentration ratio $O_2/N_2O=2\ l/5\ l$), it increased up to 540 msec. At this stage, the spontaneous EEG showed typical high-voltage slow waves with dominant frequencies 2–3 Hz as shown in Fig. 2b. Under 2.0% enflurane, the Pmax latency showed values in the range 470–503 msec. When enflurane was decreased to 1.0%, the Pmax latency was reduced to 254 msec and then to 199 msec after the recovery from anesthesia.

Figure 3 shows a case for halothane with neuro-lepto-anesthesia (NLA). The patient was 56 year-old male with body-weight 41 kg operated for Cholecystectomy. The Pmax latency was 216 msec in preanesthesia. With NLA administration of 5 mg droperidol, 100 μg fentanyl and 50 mg thiamylal, the nitrousoxide anesthesia was initiated (concentration ratio of $O_2/N_2O=2\ l/4\ l$). The Pmax value was 274–282 msec while 1.0% halothane was used, but 10 minutes after an increase of halothane up to 2.0%, a drastic increase in the Pmax latency up to 549 msec was observed. The ongoing EEG showed high-voltage slow waves at this stage. After turning-off halothane, the Pmax latency was reduced to 291 msec and returned to a preanesthetic level 216 msec, after the recovery from anesthesia.

In Fig. 4, the averaged VEP waveforms showing different Pmax latencies under enflurane anesthesia are exhibited. They were recorded from a 57 year-old female patient with body-weight 50 kg operated for Oophorectomy. The VEPs of Fig. 4 show a large positive deflection that peaks at 212, 257, 312, and 395 msec. The prolongation of the latencies can be observed to follow the increase in anesthetic concentration. Although we did not pay particular attention to changes in amplitude due to the large variability of this measure, we can see in Fig. 4 that the amplitude of the

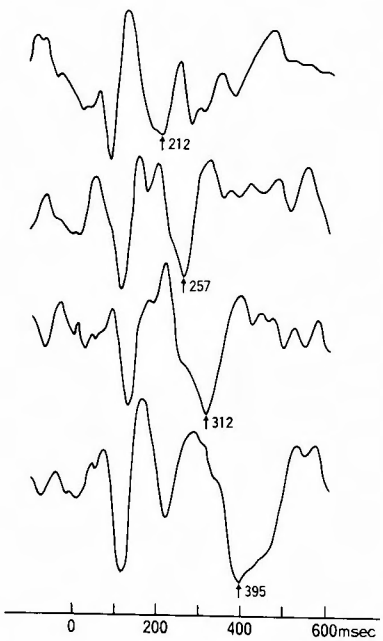

Fig. 4. Waveforms of VEP showing the prolongation of the Pmax latency under enflurane anesthesia The concentration of enflurane was changed from 0.5% to 2.0% under nitrous-oxide anesthesia with $O_2/N_2O=2\ l/4\ l$. Patient: 57 year-old female, Oophorectomy.

Pmax appears to increase with an increase in enflurane concentration.

Part (b) of Figs. 2 and 3 shows that the dominant frequency of the EEG becomes lower as the Pmax latencies increase. This tendency is illustrated in Fig. 5, where the Pmax latency is plotted against dominant frequency of the ongoing EEG for different anesthetic stages. Pmax latencies shorter than 280 msec correspond in most cases to a dominant frequency in the alpha band. Pmax latencies longer than about 500 msec correspond to dominant frequencies which lie roughly in the range 3–5 Hz. In these cases EEG traces exhibited high-voltage slow waves as shown in part (b) of Figs. 2 and 3. These results indicate that an increase in the depth of anesthesia causes changes in the EEG as well as in the VEP namely a drastic prolongation of the Pmax latency.

In Fig. 6, the Pmax latency is plotted with respect to the concentration of enflurane. A regression line was fitted to the data. The regression line is given by $y=251.8+76.5x$, where x denotes

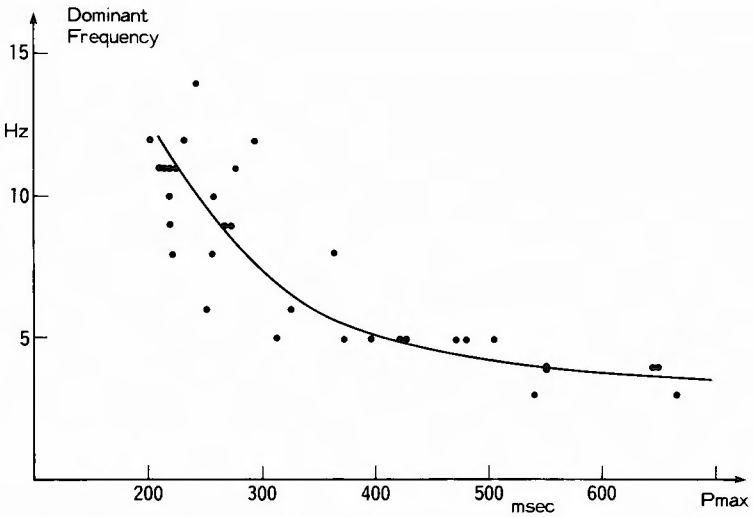

Fig. 5. Dominant frequenceis of ongoing EEG plotted against Pmax latencies. Dominant frequencies decrease according to an increase in the Pmax latency.

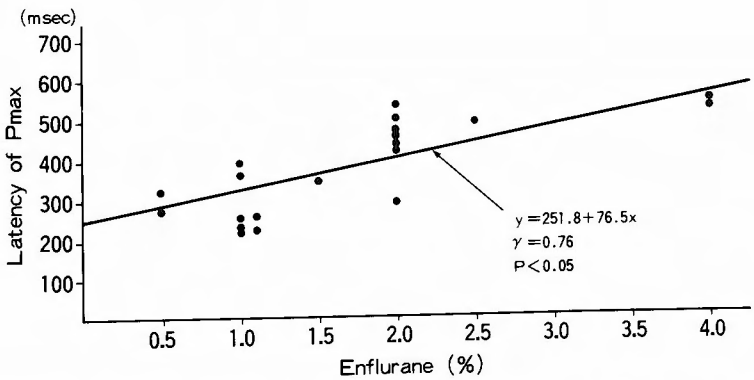

Fig. 6. Correlation between the Pmax latency of VEP and the concentration of enflurane. The ordinate shows the Pmax latency in msec and the abscissa indicates the concentration of enflurane. The solid line shows the regression line (x; concentration in %, y; the Pmax latency in msec) and γ represents the correlation coefficient. ($p<0.05$)

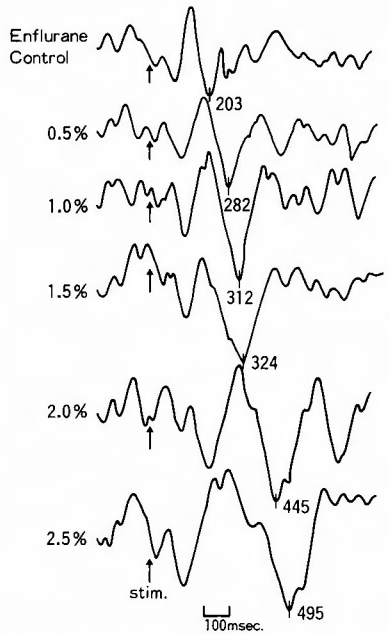

Fig. 7. Typical waveforms of the averaged VEP extracted from observed results for 4 subjects among 10 subjected to the correlation analysis in Fig. 6. The Pmax latencies show prolongations according to an increase in enflurane concentration.

the concentration in percentage and y the Pmax latency in msec. The correlation coefficient is 0.76, which demonstrates the existence of a significant correlation ($p<0.05$) between the concentration of enflurane and the Pmax latency. The data used for the correlation analysis were taken from 10 subjects (2 males and 8 females with ages from 37 to 74).

In Fig. 7, the averaged VEP waveforms are shown with respect to various values of enflurane concentration. The VEP waveforms were extracted from the data used in the correlation analysis of Fig. 6. This figure shows how the prolongation of the Pmax latency is related to the enflurane anesthesia, although the averaged VEP waveforms were extracted from those of several subjects.

Discussion

The latency of the late positive peak of the VEP was abnormally long (>250 msec) compared to normal unanesthetized subjects in the following cases: i) after administration of 1.0% enfluane for more than 20 minutes and ii) after administration of halothane at a concentration larger than 1.0%. In case of administration of droperidol etc. (NLA), the Pmax latency increased about 5 minutes after the intravenous injection of the drug but this increase was rather slight as compared to the case of inhalation of enflurane or halothane. In the case of nitrous-oxide anesthesia, the Pmax latency of VEP was only slightly prolonged. Although the anesthetic conditions were different and variable for different cases, it can be said that the Pmax latencies increased in proportion to an increase in concentration of enflurane or halothane if other conditions were kept unchanged. Arterial blood pressure and body temperature of each subject were maintained at the preanesthetic level in every case as

much as possible.

These results contrast to those found when early latency EP components are considered. This is the case of the evoked responses related to blink reflexs that correspond to early peaks at short latency. These are determined by activity in the specific sensory areas of the cerebral cortex. SUTTON et al. (1973) found that even when the EEG traces become almost isoelectric under a barbiturate (63 mg/kg), the early components of VEPs with latency 10–20 msec still celarly remain[14]. The amplitude of the early components of some types of EPs sometimes decrease as the anesthetic concentration is increased as shown, for example, by PETERSON et al. (1986) for the SSEPs[12]. These findings suggest that the early components cannot be used for monitoring of anesthesia.

The late latency componentsd of the VEP correspond most likely to the processing of visual information in multi-synaptic pathways (NAUTA, 1971; JUNG, 1973; YORK et al., 1981)[5,8,17]. Such pathways are likely affected by anesthetic drugs. Although it is possible that the prolongation of the latency of the VEP components may depend also on a peripheral effect, such an effect, for example, causing a delay on early components at the retinal level, can be regarded as small in comparison with the effect at cerebral level. Thus the finding of a significant correlation between the concentration of enflurane and the prolongation of the Pmax latency indicates a change in cerebral processes induced by anesthesia.

We should note that an averaged evoked potential includes both a true response component and uncancelled background activity and other noise components. Therefore it is necessary to remove the background activity and noise due to body movements or artefacts (e.g. due to electric scalpel) in order to obtain good estimates of evoked responses. In the present investigation, random photic stimuli were employed in order to minimize the effects of background activities (NOGAWA et al., 1973, 1976)[9,10].

In conclusion, the prolongation of the Pmax latencies does not appear to depend on the drug type used, rather on its concentration, i.e. on the depth of anesthesia, if other conditions were kept unchanged. Such a sensitivity implies that the measurement of the post-stimulus latency of VEP (the Pmax latency) can be useful for monitoring the depth of anesthesia during operation.

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Deviece: CA-5200 (Cadwell Laboratories, Inc. 1021 North Kellog, Kennewick Washington, 99336 U.S.A.) with random pulse genrator (Homer Ion Laboratory, 17–2, Shinsen, Shibuya, Tokyo 150 Japan)

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和文抄録

麻酔下視覚誘発電位の最大陽性ピーク潜時の変化

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麻酔深度の監視に視覚誘発電位 (VEP) が適応可能かどうかを吟味するために，外科手術中患者の視覚誘発電位と麻酔深度との関係を研究した．視覚誘発脳波は両耳朶を不関電極とする頭頂部中央より単極誘導で記録し，光刺激はゴーグル内に添付した発光ダイオードで両眼同時に刺激を与え，光刺激間隔は2－5秒の間に一様分布するランダムな時間間隔を用いた．加算法により光刺激時点より最大陽性ピーク潜時 (Pmax) までの潜時を評価するのに50個のデータを加算平均した．

麻酔剤の投与にともない最大陽性ピーク潜時の増大および麻酔終了後には麻酔以前の値に戻ることが見いだされた．とくに最大陽性ピーク潜時とエンフルレンガス濃度との間に有意な相関があることが示された．Pmax の潜時は覚醒状態における約 200 msec から脳波が高電位徐波を示す段階における約 600 msec まで鋭敏な延長を示した．

従って，誘発電位の Pmax 潜時の測定は麻酔深度の監視に有用であることが分かった．